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L2 with l1

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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ

<u>L3</u>	L2 with l1	58	<u>L3</u>
<u>L2</u>	molecular weight or MW	646741	<u>L2</u>
<u>L1</u>	DSPG or DSPE or phosphatidyl glycerol	1123	<u>L1</u>

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L3: Entry 19 of 58

File: USPT

Apr 17, 2001

DOCUMENT-IDENTIFIER: US 6217886 B1

TITLE: Materials and methods for making improved micelle compositions

Detailed Description Paragraph Right (50):

DSPE-PEG (16.5 mg, molecular weight 2748.01) was placed in a 20 ml glass vial and 6 ml saline buffer was added to give a final DSPE-PEG concentration of 1.0 $\mu\text{mol/ml}$. The mixture was vortexed for one minute until the solution was clear, after which the vial was topped with argon and sealed with parafilm. The mixture was allowed to stand at room temperature for one hour or until the bubbles rose out of the mixture. The resulting micelle solution was designated "S1". Twelve μg human galanin (molecular weight 3158.1) was placed in a polypropylene tube and 5 ml of the S1 micelle preparation was added to the tube giving a final galanin concentration of 1 nmol/1.4 ml. The mixture was vortexed for ten seconds and incubated at room temperature for two hours. The size of the resulting galanin containing micelles, 17 to 20 nm, was measured by QELS as described in Example 3.

Detailed Description Paragraph Right (51):

According to the present example, micelle composed of two different compositions were prepared and characterized in order to determine an optimal system for increasing solubility of normally water-insoluble compounds. In the first system, micelles were composed of DSPE-PEG and PC. When DSPE-PEG is mixed with phosphatidylcholine (PC) in aqueous medium, mixed micelles are formed instead of liposome bilayers. In the second system, micelles were formed using PC in combination with a representative bile salt, sodium taurocholate (Sigma). When small molecular weight surfactants, such as bile salts, are mixed with DSPE-PEG, formation of spherical mixed micelles can also be detected. The purpose of this study was (i) to compare the effect of DSPE-PEG and bile salts on phosphatidylcholine (PC) capacity to form mixed micelles; (ii) to examine and compare characteristics of the resulting mixed micelles, including micelle-to-vesicle-transition upon dilution; and (iii) to compare solubilization potential of the two micelle systems.

1.85 $\times 10^{-5}$
2.8 $\times 10^{-5}$

1.82
2.8
1.7 $\times 10^{-5}$
2.51 $\times 10^{-4}$

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L3: Entry 42 of 58

File: USPT

Dec 2, 1997

DOCUMENT-IDENTIFIER: US 5693769 A

TITLE: Glycosylated steroid derivatives for transport across biological membranes and process for making and using same

Detailed Description Paragraph Right (98):

To a 25 mL round bottom flask 20.5 mg egg yolk (Sigma, average MW 770.4) dissolved in CHCl₃/MeOH, 5.0 mg phosphatidyl glycerol (Sigma, MW 772) dissolved in CHCl₃/MeOH, and 12.7 mg repurified cholesterol (Aldrich, MW 386.66) were added. The molar ratio of egg yolk; phosphatidyl glycerol:cholesterol was 4:1:5 (66 moles total lipid). The solvent was removed on a rotary evaporator. The dried lipid mixture was then put under argon and 3 mL freshly distilled diethyl ether was added. After the lipid had redissolved, 1 mL of carboxyfluorescein dissolved in water (pH adjusted to 7.4) was added to a concentration of 180 mM (the concentration of carboxyfluorescein was determined by UV; the extinction coefficient at pH 7.4 is 5.6.times.10.sup.4 ; .lambda..sub.max =492). The lipid mixture containing carboxyfluorescein was sonicated under argon in a bath type sonicator at 5.degree.-15.degree. C. for 15-30 minutes. The mixture was then placed on the rotary evaporator and the organic solvent was removed. To separate the carboxyfluoresceinloaded vesicles from unencapsulated carboxyfluorescein, the remaining aqueous vesicle mixture was loaded on a Sephadex G-25 column equilibrated with 145 mM NaCl/10 mM Hepes at pH 7.4. The carboxyfluorescein-loaded vesicles eluted in the first fraction after the void volume while the unencapsulated carboxyfluorescein remained on the column. The purified vesicles were diluted with 145 mM NaCl/10 mM Hepes buffer (pH 7.4) until the fluorescent intensity of the vesicle mixture measured approximately 10.

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L3: Entry 9 of 58

File: PGPB

Nov 8, 2001

DOCUMENT-IDENTIFIER: US 20010038851 A1

TITLE: Therapeutic liposome composition and method of preparation

Detail Description Paragraph (94):

[0132] The Fab fragments (molecular weight of 3,000 Daltons) were mixed in a 1:1 molar ratio with PEG-DSPE (molecular weight 50,000 daltons) having an active maleimide end group (prepared as described in U.S. Pat. No. 5,527,528). The two components were incubated overnight at room temperature. The unreacted maleimide was quenched with 2 mM .beta.-mercaptoethanol for 30 minutes at room temperature. The free Fab fragments and .beta.-mercaptoethanol were separated from the Fab-PEG-DSPE conjugate on an S-200 column equilibrated in 25 mM HEPES/0.9%saline at pH 7.2. Fractions of 1 ml were collected and read on the spectrophotometer at 280 nm to determine the fractions containing the conjugate and the free Fab fragments. The fractions were pooled accordingly and the concentration of the Fab-PEG-DSPE micellular solution is determined spectrophotometrically (280 nm). The efficiency of conjugation of the Fab fragment to the maleimide-PEG-DSPE was approximately 40%.

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L3: Entry 1 of 58

File: PGPB

Apr 25, 2002

DOCUMENT-IDENTIFIER: US 20020048596 A1

TITLE: PREPARATION FOR THE TRANSPORT OF AN ACTIVE SUBSTANCE ACROSS BARRIERS

Detail Description Paragraph (81):

[0110] Mixtures of SPC (molecular weight assumed to be 800 Da) with increasing amounts of 0, 30 and 40 mole percent DSPE-PEG (molecular weight assumed to be 5800 Da) and pure DSPE-PEG liposomes not containing any SPC are prepared. Subsequently, the mixtures obtained were dissolved in a chloroform/ methanol solution. After that, the lipid solution is transferred to a round-bottom flask. After removal of the solvent in a rotary evaporator, a thin lipid film remains behind on the wall of the flask. This film is dried further under vacuum (10 Pa), subsequently hydrated by addition of buffer and suspended by mechanical stirring. A cloudy suspension is obtained which, as a rule, is very viscous. The size of the particles in the resulting suspension is determined by means of dynamic light scattering as well as by means of microscopy. In all cases, the particle size observed is always greater than 0.5 μm . Therefore, for the mixtures investigated, micelle formation and consequently also solubilization can be excluded by means of dynamic light scattering.